AMERICAN HERBAL PRODUCTS ASSOCIATION

February 10, 1999

DELIVERED BY COURRIER

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

Re: Docket No. 98N-0148
64 Federal Register 1629 (Jan. 11, 1999)

COMMENTS OF THE AMERICAN HERBAL PRODUCTS ASSOCIATION

To Whom It May Concern:

These comments are submitted on behalf of the American Herbal Products Association ("AHPA") for consideration by the Food and Drug Administration ("FDA") in preparing the position of the United States on the World Health Organization's ("WHO") proposal to add ephedrine to Schedule IV of the 1971 United Nations Convention on Psychotropic Substances ("1971 Convention"). AHPA objects to the WHO's recommendation generally and objects specifically as it applies, if at all, to herbal ephedra products.

Summary of AHPA's Position

The WHO's recommendation for scheduling of ephedrine is based upon little or no scientific evidence. AHPA believes the factual record in support of the WHO's recommendation is inconclusive with regard to ephedrine and completely lacking with regard to dietary supplements that contain herbal ephedra. No apparent distinction has been made in the recommendation between ephedrine and herbal ephedra, despite significant differences in the potential for abuse or misuse of the substances. Herbal ephedra is widely and beneficially used in the United States and throughout the world in lawful food and dietary supplement products without the risks of dependence and abuse that are the focus of the 1971 Convention.

The WHO's concern regarding ephedrine focuses on the ingredient's potential use as a precursor in the manufacture of methamphetamines, rather than on its potential for abuse. The potential use of a substance as a precursor ingredient should be irrelevant

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to the decision to schedule a substance under the 1971 Convention because the 1971 Convention deals with substances that have the potential for abuse, not substances that are primarily of concern because of their potential use in illicit drug traffic. The 1988 United Nations Convention Against Illicit Traffic in Narcotic Drugs and Psychotropic Substances ("1988 Convention") was adopted to deal with the latter problem and

ephedrine is, in fact, among the substances controlled under that Convention. Thus, the 1988 Convention, not the 1971 Convention, is the proper mechanism to address the WHO's precursor concerns.

The Federal government and the various states are all actively involved in the very issues apparently driving the WHO's recommendation and it is incumbent on the United States representatives to the Commission on Narcotic Drugs Meeting ("CND Meeting") in Vienna to present a position consistent with United State's domestic policy. That policy is manifest in the Dietary Supplement Health and Education Act ("DSHEA"), the Controlled Substances Act ("CSA") and various amendments thereto, recent rules and proposed rules promulgated by the FDA and the DEA, as well as recent legislative action taken by various states. These domestic efforts make it clear that the question of alleged abuse of ephedra within the United States and the proper response to such abuse, if any, is being adequately addressed within the United States itself. It is therefore incumbent on the U.S. Representatives to the CND Meeting to present a position consistent with current U.S. policy. Contrary to the WHO recommendation, such policy does not require or even contemplate a doctor's prescription before products containing ephedrine or herbal ephedra can be sold.

Lastly, the U.S. Representatives to the CND Meeting are obligated to vigorously oppose the WHO recommendation because of the severe and detrimental impact the proposed scheduling of ephedrine would have on both consumers and business in this country. Our representatives to the CND Meeting have a responsibility to protect the United State's legitimate economic concerns, including protecting the interests of consumers and small businesses. In short, our representatives to this meeting must not allow international regulation to curtail legitimate economic activity when the United States itself has found it unnecessary to do so.

WHO's Position Lacks Scientific Support

There is no satisfactory basis for the findings required, under Article 2, paragraph 4 of the 1971 Convention, to justify scheduling herbal ephedra as a controlled substance. Paragraph 4 states:

> (4) If the World Health Organization finds:
> (a) That the substance has the capacity to produce
> (i)(1) a state of dependence, and

(2) central nervous system stimulation or depression, resulting in hallucinations or disturbances in motor function or thinking behavior or perception or mood, and

(b) that there is sufficient evidence that the substance is being or is likely to be abused so as to constitute a public health and social problem warranting the placing of the substance under international control,

the World Health Organization shall communicate to the Commission an assessment of the substance, including the extent or likelihood of abuse, the degree of seriousness of the public health and social problem and the degree of usefulness of the substance in medical therapy, together with recommendations on control measures, if any, that would be appropriate in the light of this assessment."

Although some countries have reported past or present abuse of ephedrine, these reports primarily focus on synthetic and/or pure ephedrine single ingredient products. There is little or no evidence that multi-ingredient ephedrine, herbal ephedra, or dietary supplements containing herbal ephedra are subject to abuse. Furthermore, there is no mention of abuse of herbal ephedra in DEA's April 17, 1998 comments to FDA regarding abuse and trafficking data for ephedrine. In fact, the WHO itself has acknowledged the distinction between ephedrine and herbal ephedra. The WHO noted that "when abuse exists, it seems to involve ephedrine single entity products." Unfortunately, its recommendation fails to exempt herbal ephedra from the proposed scheduling.

Regardless of the findings regarding ephedrine, herbal ephedra, due to significant distinctions from ephedrine, meets none of the criteria required for it to be considered for scheduling under the 1971 Convention. According to the criteria set forth above, in order for herbal ephedra to be scheduled under the 1971 Convention, it must be established that the substance is (1) capable of producing a state of dependence; (2) capable of producing central nervous system stimulation or depression, resulting is hallucinations or disturbances in motor function or thinking behavior or perception or mood; and (3) likely to be abused so as to constitute a public health and social problem. The WHO has failed to establish these criteria. There is simply no evidence that dietary supplements containing herbal ephedra produce a state of dependence, nor is there any evidence of addiction to these products. Dietary supplements have not been known to cause hallucinations or disturbances in motor function. Indeed, an in-depth review of adverse reaction reports on which the FDA has relied for past rule making casts considerable doubt on their reliability as a basis for such regulation. Therefore, given the lack of evidence of abuse of herbal ephedra, the WHO has no legitimate basis for concluding that herbal ephedra constitutes a public health and social problem justifying scheduling according to the 1971 Convention. Consequently, herbal ephedra and dietary

supplements that contain herbal ephedra should be exempted from scheduling even if ephedrine is added to any schedule under the 1971 Convention.

The 1988 Convention is the Proper Mechanism to Address Concerns Regarding the Use of Ephedrine or Herbal Ephedra as Precursors

Ephedrine is listed in Table 1 of the 1988 Convention as a precursor chemical. The 1988 Convention was enacted to reinforce and supplement the 1971 Convention to more effectively address the illicit production of, demand for, and traffic in narcotic drugs and psychotropic substances. The 1971 Convention, on the other hand, focuses on the risks associated with the scheduled substances themselves. As described above, herbal ephedra does not meet the criteria for scheduling under the 1971 Convention.

The 1988 Convention identifies a number a measures to be adopted by the parties to prevent the diversion of listed substances, including, among others:

- establishing a system to monitor the international trade of listed substances;
- authority to seize listed substances if evidence shows they are being used as a precursor;
- labeling and documentation requirements for imports and exports of listed substances;
- record-keeping requirements for imports and exports of listed substances.

Thus, new concerns regarding the diversion of ephedrine for the illicit manufacture of drugs or psychotropic substances could be fully addressed by the 1988 Convention. No problem of this type exists for dietary supplements containing herbal ephedra. Further, the United States, as well as other parties to the Convention continue to take action to ensure that their domestic policies fully incorporate the provisions of the 1988 Convention. In the U.S., the Domestic Chemical Diversion Control Act ("DCDCA") was enacted in 1993 and the DEA has recently proposed regulations seeking to implement the DCDCA in prevention of chemical mixtures containing listed substances.

Adding ephedrine to Schedule IV of the 1971 Convention, when it is already listed in and regulated by the 1988 Convention, will create confusion among the parties to the 1971 Convention and make enforcement of any restrictions on ephedrine troublesome. For example, it is unclear whether regulatory requirements (such as labeling and record keeping for imports and exports) and tools (such as authority to seize listed substances used as precursors) applicable to ephedrine under the 1988 Convention would still apply if the substance is scheduled as a controlled substance under the 1971 Convention. As the Expert Committee pointed out in its recommendation, the overlapping jurisdictions of the two Conventions would likely make "full effective international regulations of ephedrine difficult." The United States should not support international regulations when the domestic impact of those regulations is unclear due to

the confusion regarding the jurisdiction of the Conventions. In any event, it is clear that neither Convention's jurisdiction should extend to the regulation of herbal ephedra.

Current Domestic Regulations Within the United States Are Adequately Addressing Any Issues of Ephedrine Abuse and United States International Policy Should Be Consistent with its Domestic Policy

To prevent disruption of the current U.S. regulatory scheme, to preserve sovereignty, and to ensure consistency in its domestic and international policies, the United States should vote against any scheduling of ephedrine, and particularly herbal ephedra, under the 1971 Convention. The laws and regulations in place in the United States addressing ephedrine or herbal ephedra follow the provisions set forth in the 1988

Convention by focusing on the potential of substances as precursors in the manufacure of methamphetamines. The United State has not sought further international restriction on ephedrine because of a domestic policy decision to protect consumer access to effective

OTC drug and dietary supplement products containing ephedrine or herbal ephedra. The thrust of U.S. laws that address ephedrine or herbal ephedra involve diversion, not abuse. The United State's position at the CND Meeting should be consistent with this well-expressed and well-established policy. Problems with diversion of ephedrine, which do not relate to herbal ephedra, have already been handled domestically through the registration controls placed on these products at state and federal levels. Broad restrictions that would result from scheduling under the 1971 Convention are unwarranted, unjustified and devoid of factual support.

The proposed scheduling to ephedrine as a Schedule IV controlled substance by the UN could require the implementation of regulations in the U.S. to fully incorporate the provisions of the 1971 Convention, including medical prescriptions to dispense ephedrine as well as licenses for manufacturers, distributors, and retailers of ephedrine products. The regulatory requirements contradict Congressional intent as reflected in DSHEA (as to herbal ephedra) and in the Controlled Substances Act (as to ephedine). Simply put, the policy of the United States on any international attempt to regulate ephedrine and herbal ephedra beyond what the United States has done domestically should reflect Congressional intent and it has never been the intent of Congress to require prescriptions for lawful OTC and dietary supplements containing ephedrine and herbal ephedra. Therefore, the U.S. representatives to the CND Meeting must oppose the WHO recommendation.

Adoption and Implementation of the WHO Recommendation Will Have Severe and Unwarranted Economic Consequences in the United States

Under Article 2, paragraph 5 of the 1971 convention, the CND is to consider economic and social factors, among others, when determining whether to add a substance

to any scheduling. The U.S. should consider the detrimental impact the proposed scheduling of ephedrine will have on both consumers and businesses in this country. The proposed scheduling of ephedrine would restrict consumer access to products containing pure or synthetic ephedrine, such as bronchodilators, that FDA has concluded are safe for OTC use when properly labeled and taken as directed. Furthermore, over five million people consume dietary supplements containing ephedra in the U.S. each year according to conservative estimates. If ephedrine is added to Schedule IV of the 1971 Convention, these millions of consumers would be prohibited from obtaining dietary supplements that contain ephedra—even if sold for a lawful and beneficial purpose—without a prescription, if they could be obtained at all.

The impact of scheduling of ephedrine on U.S. businesses that manufacture or distribute ephedrine and herbal ephedra-containing products would be equally severe. FDA has estimated that there are between 200 and 5,000 products containing ephedrine alkaloids on the market. According to estimates by the dietary supplement industry, several hundred thousand small businesses (including independent distributors and retailers) will be impacted by the proposed scheduling. Many of these businesses are small businesses, according to comments from the Small Business Administration to FDA in response to FDA's proposed rule for dietary supplements containing ephedrine alkaloids.

Conclusion

Scheduling of ephedrine or herbal ephedra under the 1971 Convention is misguided and unnecessary. The factual record for ephedrine does not support the conclusion that the substance should be scheduled as a controlled substance under the 1971 Convention. If, however, ephedrine is added to any schedule under the 1971 Convention, herbal ephedra and dietary supplements containing herbal ephedra should not be scheduled. There is simply no evidence that herbal ephedra produces a state of dependence or addiction and therefore the basic scheduling requirements of the 1971 Convention are simply not met with regard to this substance.

Next, the potential use of a substance as a precursor should not be considered in a scheduling decision under the 1971 Convention, the purpose of which is to address the abuse potential of a substance. The 1988 Convention is the proper means to address precursor use and already includes ephedrine as a regulated substance. Furthermore, the U.S. has a regulatory scheme in place to adequately address any legitimate concerns regarding the precursor use of a substance.

Lastly, AHPA urges the United States to take into consideration the impact of restricting the access of millions of consumers to ephedra and products containing ephedra. AHPA believes that the United States' international policy on regulation of ephedrine should be consistent with its domestic policy and that the U.S. Representatives to the CND Meeting have a duty to do all that they can to further an international policy

consistent with existing U.S. domestic policy. The WHO recommendation is not consistent with existing U.S. domestic policy. In fact, the recommendation if adopted would re-write such policy altogether. Therefore the WHO recommendation should and must be rejected by the U.S. delegation to the CND Meeting.

Respectfully Submitted,

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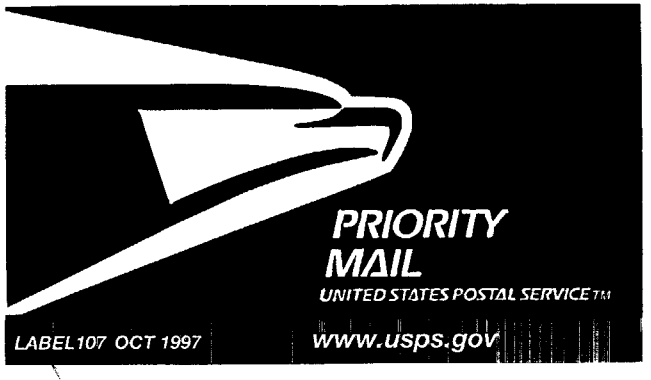

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